REMARKS

Claims 1, 3-6, and 8-36 were pending at the time of the Office Action. Claims 33 and 34 have been withdrawn from consideration. Claims 1, 4-5, and 8-20 stand rejected under 35 U.S.C. § 102. Claims 1, 3-6, 8-32, 35, and 36 stand rejected under 35 U.S.C. § 103. Claims 1, 6, 8-32, and 36 are also provisionally rejected for nonstatutory obviousness-type double patenting. Applicant addresses these rejections as follows.

Claim Amendments

Claim 1 has been amended to feature a method for treating a non-virally induced pre-cancerous lesion of the skin of a patient by topically administering a pharmaceutically effective amount of a polyphenol to the patient. Support for this amendment is found, for example, in claims 3 and 29, now cancelled, and at page 5, lines 8-19, and page 17, lines 24-25, of the specification as filed.

Claims 3 and 29 have been cancelled without prejudice.

The present amendments were made solely to expedite prosecution, and Applicant reserves the right to pursue any cancelled subject matter in this or in a continuing application. No new matter has been added.

Rejection under 35 U.S.C. § 102

Claims 1, 4-5, and 8-20 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Yanaga et al. (*International Journal of Molecular Medicine* 10: 311-315, 2002; herein "Yanaga"), as evidenced by Dou et al. (U.S. Patent Application Publication No. 2002/0151582; herein "Dou"). According to the Examiner, Yanaga teaches that "EGCG inhibited growth in the mouse viral mammary epithelial carcinogenesis model RIII/MG, and induced apoptosis, suggesting a clinical usefulness of EGCG as a chemopreventive substance" (Office Action, page 4). The Examiner cites Dou as evidentiary support that the green tea extracts of Yanaga contain polyphenolic compounds (e.g., EGCG).

To expedite prosecution, Applicant has amended claim 1 to feature a method for treating a non-virally induced pre-cancerous lesion of the skin of a patient (e.g., actinic keratoses) by topically administering a pharmaceutically effective amount of a polyphenol to the patient. The Examiner has conceded that Yanaga does not discuss a non-virally induced pre-cancerous skin lesion. Furthermore, Applicant notes that Yanaga fails to teach that a polyphenol may be administered topically. Indeed, the experiments of Yanaga describe the ingestion of a catechin composition rather than topical administration. Applicant submits that the rejection of claims 1, 4-5, and 8-20 under 35 U.S.C. § 102(b) should be withdrawn.

Rejection under 35 U.S.C. § 103

Claims 1, 4-5, and 8-26 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Yanaga, as evidenced by Dou. This rejection is respectfully traversed. As described above, Applicant has amended independent claim 1 to feature a method for treating a non-virally induced pre-cancerous lesion of the skin of a patient by topically administering a pharmaceutically effective amount of a polyphenol to the patient. The Examiner has conceded that Yanaga fails to teach or suggest treatment of a non-virally induced pre-cancerous skin lesion by administering a pharmaceutically effective amount of a polyphenol, as recited in amended claim 1 or its dependent claims, and Dou does not cure this deficiency. Accordingly, Applicant respectfully requests that this first rejection of the claims under 35 U.S.C. § 103(a) be withdrawn.

Claims 1, 4-6, 8-32, and 35 also stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Yanaga in view of Brash et al. (U.S. Patent Application Publication No. 2002/0198161; herein "Brash") and further in view of Voet (U.S. Patent No. 6,723,750; herein "Voet"), as evidenced by Dou. Brash and Voet fail to cure the deficiencies of Yanaga, as neither indicates that polyphenol-containing compounds treat non-virally induced pre-cancerous lesions of the skin. Reconsideration and withdrawal of this second basis for the rejection is also respectfully requested.

Claims 1, 4-6, 8-20, and 36 stand further rejected under 35 U.S.C. § 103(a) as being unpatentable over Yanaga and Dou in view of An et al. (*Photochemistry and Photobiology* 76: 73-80, 2002; herein "An"). The Examiner states (Office Action, pages 10-11):

> It would have been *prima facie* obvious for one of ordinary skill in the art at the time the invention was made to use the green tea extract to treat actinic keratoses from [An] since [An] teach[es] green tea extract (1 mg/cm^2) largely abrogated the acute COX-2 response to UVB in mice or humans.

Applicant submits that An fails to cure the deficiencies of Yanaga, as An does not teach or suggest the treatment of non-virally induced pre-cancerous lesions of the skin, such as actinic keratoses. An teaches the topical administration of green tea polyphenol (GTP) extract to murine or human skin prior to UVB irradiation, resulting in the subsequent attenuation of COX-2 expression in the treated cells. An fails to teach or suggest that GTP extract treats an established lesion (e.g., actinic keratoses). Indeed, An states (pages 78-79):

> [T]he observed decrease in COX-2 expression in both murine and human skin receiving a topical application of GTP suggests that GTP may act as a chemopreventive agent by blocking this target.

Accordingly, Applicant respectfully requests that this rejection of claims 1, 4-6, 8-20, and 36 under 35 U.S.C. § 103(a) be withdrawn.

Claims 1, 3-6, 8-32, and 35 also stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Yanaga, Dou, Brash, Voet, and further in view of Araki et al. (*Annals of the New York Academy of Sciences* 768: 215-222, 1995; herein "Araki"). As described above, Yanaga, Dou, Brash and Voet, alone or in combination, do not teach a method for treating a non-virally induced pre-cancerous lesion by administering a pharmaceutically effective amount of a polyphenol. Araki does not cure the deficiencies of these references.

The Examiner states (Office Action, page 14):

> It would have been *prima facie* obvious for one of ordinary skill in the art at the time the invention was made to use EGCG to treat oncogene-initiated

RIII/MG cells since Araki et al teach EGCG is effective in both oncogene or virus initiated MMEC/myc3 and RIII/MG cells. Since all the references teach using green tea extract to treat precancerous lesion, one of ordinary skill in the art would have been motivated to make the modifications and combine the references together.

Araki does not cure the deficiencies of Yanaga, Brash, Voet or Dou, as Araki does not teach or suggest the treatment of non-virally induced pre-cancerous lesions of the skin. Instead, Araki teaches EGCG-treatment of two mammary epithelial cell lines: a stable c-myc transfectant MMEC/myc$_3$ strain and a murine mammary tumor virus (MTV)-expressing RIII/MG strain. The RII/MG cell line is virally induced, and the MMEC/myc$_3$ cells are derived from murine mammary glands, as described in Telang et al. (*Cell Regulation* 1: 863-872, 1990; herein "Telang") and submitted herewith. Telang states (page 870, last paragraph, under "Materials and methods") that "[t]he mouse mammary epithelial cell line MMEC was established from 8-wk-old virgin BALB/c mice. The inguinal (#4) mammary glands from eight animals were pooled and finely minced with scalpels." The tissue was digested and cultured, thereby resulting in the establishment of the MMEC cell line. The mammary gland cells of the MMEC/myc$_3$ cell line are epithelial cells and not skin cells; however, the Examiner has inappropriately equated skin cells with epithelial cells. As Applicant notes in the specification, skin is the body's largest organ and protects against heat, sunlight, injury, and infection (page 1, lines 14-15, of the specification as filed). Thus, skin, as it relates to the present invention, refers to skin as an organ and not to epithelial cells in general. Viral carcinogenesis of MMEC/myc$_3$ cells (i.e., mammary gland epithelial cells) would not result in the development of a pre-cancerous skin lesion. Furthermore, amended claim 1 or claims dependent therefrom requires that the polyphenol be administered topically. It is clear that cells of the mammary glands cannot be treated topically. Applicant respectfully requests that this rejection of claims 1, 3-6, 8-32, and 35 under 35 U.S.C. § 103(a) be withdrawn.

Provisional Double-Patenting Rejection

Claims 1, 6, 8-32, and 36 stand provisionally rejected for obviousness-type double patenting over claims 1-6, 8, 16, 18, 23-27, and 30-33 of co-pending U.S. Patent Application Serial No. 10/682,612. Applicant requests that this rejection be held in abeyance until the pending claims are found to be otherwise allowable except for these grounds of rejection.

CONCLUSION

Applicant submits that the claims are now in condition for allowance, and such action is respectfully requested. Transmitted herewith is a Petition to extend the period for replying to the Office Action for one month, to and including March 22, 2010 (as March 20, 2010 was a Saturday), and payment of the required extension fee.

If there are any other charges or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

Date: 22 March 2010

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